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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,819	10/11/2006	Richard Heng	33739-US-PCT	5179

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,819	HENG ET AL.	
	Examiner	Art Unit	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

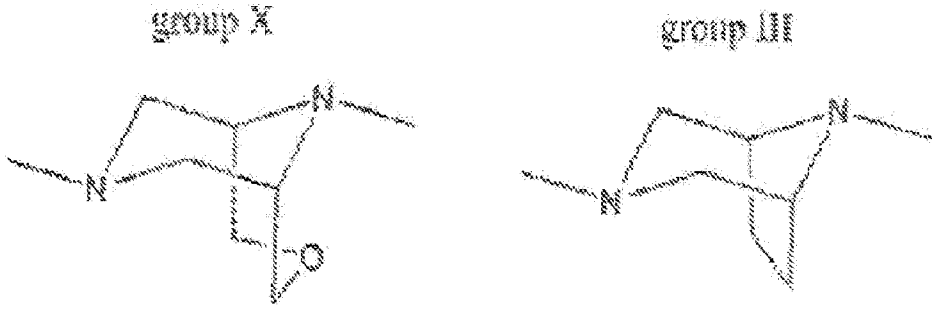
1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are pending in the application.

Election/Restrictions

1. Applicant's election with traverse of Group X in the reply filed on November 2, 2009 is acknowledged. The traversal is on the ground(s) that Groups X and III do form one single group of inventions within the meaning of R. 13.1 and R. 13.2 PCT. All compounds of these “three" groups relate to bridged piperazine derivatives. The difference is that the bridge is a residue -CH_2-O-CH_2- {group X), vs. a residue -CH_2-CH_2- (group III). Contrary to the examiners opinion, these two groups do not contain a significantly different chemical structure: starting from group III {enthenyl bridge) to arrive at group X means to insert one oxygen atom in the chain. The differences / similarities of these two groups are shown in the structural formula below:



This is not found persuasive because first the two groups III and X are a 5-6 ring system and a 6-6 ring system, respectively. They are consequently separately classified in the U.S. Patent Classification System and require separate searches in the Chemical literature. None of the prior art considers these groups as functional equivalents. Each group can support a patent. One does not require the other for their

use. The compounds of Group III are classified in class 544, subclass 349 with the piperazines, however Group X is classified in class 544, subclass 105 with the 1,4-oxazines. A search of the elected Group X yielded 1924 patents in the U.S. Classification System. If, say, the 3,8-diazabicyclo[3.2.1]oct-3-yl compounds of Group III, were anticipated, applicants would not acquiesce in the objection of Group X there over or vice-versa and, thus, they are not linked to the same or corresponding special technical features. For example WO 2002/032901 anticipates the compounds of Group III, but not the compounds of Group X.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 8, 9, 11 and 13-15 are rejected under 35 U.S.C. 1 12, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In evaluating the enablement question, several factors are to be considered. In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988)., Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The scope of

the method claims are not adequately enabled solely based on the inhibition of the chemokine receptors provided in the specification. Instant claim language embraces disorders not only for treatment, but, for prevention which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop HIV and/or AIDS. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of in vivo efficacy by those skilled in the art. See In re Ruskin, 148 USPQ 221., Ex parte Jovanovics, 211 USPQ 907., MPEP 2164.05(a). Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQZd 1001.

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQ2d 1001.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by “optionally substituted oxy”, which is indicated to be a divalent radical in the definition of R1, R2 and R3 as well as the definition of R4.

b. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by “carbonyl”, which is indicated to be a divalent radical in the definition of R1, R2 and R3 as well as the definition of R4.

c. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by “sulfur”, which is an atom not a substituent in the definition of R1, R2 and R3 as well as the definition of R4.

d. Regarding claim 1, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). See the definitions of R1, R2 and R3 as well as the definition of R4.

e. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by “carbonyl” and “sulfonyl”, which is indicated to be a divalent radical in the definition of R.

f. Claim 1 recites the limitation "CH" in the definition of Q in the limitation wherein when Z is N, Q is CH. There is insufficient antecedent basis for this limitation in the claim.

g. Claim 1 is vague and indefinite in that it is not known what is meant by the range R1-R4 which does not set forth that which is included within the range.

h. Regarding claim 1, the phrase "e.g." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). See the definitions of the substituents on "R1-R4" and the substituents on the substituents.

i. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "optionally substituted oxy", which is indicated to be a divalent radical in the definition of the substituents of "R1-R4" and the substituents on the substituents.

j. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "sulfonyl, sulfonyl", which is indicated to be a divalent radical in the definition of the substituents of "R1-R4".

k. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "sulfur", which is an atom not a substituent in the definition of the substituents of "R1-R4" and the substituents on the substituents.

l. Claim 2 recites the limitation "amide, guanidine, sulfonyl, sulfonamide" in the definition of R1. There is insufficient antecedent basis for this limitation in the claim.

m. Claim 2 is vague and indefinite in that it is not known what is meant by “optionally substituted oxy”, which is indicated to be a divalent radical in the definition of the substituents of R1 and the substituents on the substituents.

n. Claim 2 recites the limitation "heterocycloalkyl" in the definition of the substituents of R1. There is insufficient antecedent basis for this limitation in the claim.

o. Claim 2 is vague and indefinite in that it is not known what is meant by “sulfonyl, sulfonyl”, which is indicated to be a divalent radical in the definition of the substituents of R1.

p. Claim 2 is vague and indefinite in that it is not known what is meant by “sulfur”, which is an atom not a substituent in the definition of the substituents of R1 and the substituents on the substituents.

q. Claim 4 is vague and indefinite in that it is not known what is meant by “optionally substituted oxy”, which is indicated to be a divalent radical in the definition of R1” and R2”.

r. Claim 4 is vague and indefinite in that it is not known what is meant by “carbonyl”, which is indicated to be a divalent radical in the definition of R1” and R2”.

s. Claim 4 is vague and indefinite in that it is not known what is meant by “sulfur”, which is an atom not a substituent in the definition of R1” and R2”.

t. Regarding claim 4, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). See the definitions of R1" and R2".

u. Claim 4 is vague and indefinite in that it is not known what is meant by "carbonyl" and "sulfonyl", which is indicated to be a divalent radical in the definition of R.

v. Claim 4 recites the limitation "CH" in the definition of Q" in the limitation wherein when Z" is N, Q" is CH. There is insufficient antecedent basis for this limitation in the claim.

w. Regarding claim 4, the phrase "e.g." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). See the definitions of the substituents on R1" and R2" and the substituents on the substituents.

x. Claim 4 is vague and indefinite in that it is not known what is meant by "optionally substituted oxy", which is indicated to be a divalent radical in the definition of the substituents of R1" and R2" and the substituents on the substituents.

y. Claim 4 is vague and indefinite in that it is not known what is meant by "sulfonyl, sulfonyl", which is indicated to be a divalent radical in the definition of the substituents of R1" and R2".

z. Claim 4 is vague and indefinite in that it is not known what is meant by "sulfur", which is an atom not a substituent in the definition of the substituents of R1" and R2" and the substituents on the substituents.

aa. Claim 5 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "optionally substituted oxy", which is indicated to be a divalent radical in the definition of R_1', R_2' and R_3' as well as the definition of R_4'.

bb. Claim 5 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "carbonyl", which is indicated to be a divalent radical in the definition of R_1', R_2' and R_3' as well as the definition of R_4'.

cc. Claim 5 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "sulfur", which is an atom not a substituent in the definition of R_1', R_2' and R_3' as well as the definition of R_4'.

dd. Regarding claim 5, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). See the definitions of R_1', R_2' and R_3' as well as the definition of R_4'.

ee. Claim 5 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "carbonyl" and "sulfonyl", which is indicated to be a divalent radical in the definition of R.

ff. Claim 5 is vague and indefinite in that it is not known what is meant by the range R_1'-R_4' which does not set forth that which is included within the range.

gg. Claim 5 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "optionally substituted oxy", which is indicated to be a divalent radical in the definition of the substituents of " R_1'-R_4' " and the substituents on the substituents.

hh. Claim 5 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "sulfonyl, sulfonyl", which is indicated to be a divalent radical in the definition of the substituents of " R_1'-R_4' ".

ii. Claim 5 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "sulfur", which is an atom not a substituent in the definition of the substituents of " R_1'-R_4' " and the substituents on the substituents.

jj. Claim 7 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "formula I, Ia, II, Ib or IIb" where there are no formulas in this independent claim.

kk. Claim 8 is a substantial duplicate of claim 1 as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.

ll. Claim 9 is a substantial duplicate of claim 1 as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.

mm. Claim 10 is a substantial duplicate of claim 7 as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.

nn. Claim 11 is vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by a chemokine receptor. It is unclear which diseases are associated with each of the chemokine receptors. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties in vitro, when administered to a patient with a certain disease, does not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to

work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital -- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus iv or in a time release po formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active in vitro, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of which are inhibitors in vitro, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property, which the second drug is capable. It is common for a drug, particularly in cancer and CNS diseases, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation

shown to affect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy, which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the ad cannot determine the actual scope of the claim. Hence, the claim is indefinite.

oo. Claim 12 is a substantial duplicate of claim 7 as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.

pp. Claim 13 is a substantial duplicate of claim 1 as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.

qq. Claims 12, 14 and 15 provides for the use of a compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite

where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

rr. Claim 16 is a substantial duplicate of claim 7 as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.

ss. Claim 17 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "formula II, Ia, Ib or IIb" where there are no formulas in this independent claim.

tt. Claim 17 is vague and indefinite in that it is not known what is meant by the variables R1, R2 and R3 in formula IV which are not defined within the claim.

uu. Claim 17 is vague and indefinite in that it is not known what is meant by the variables Y, Z, Q and R4 in formula V which are not defined within the claim.

vv. Claim 17 is vague and indefinite in that it is not known what is meant by the variables R1, R2, R3, Y, Z, Q and R4 in formula I which are not defined within the claim.

ww. Claim 17 is vague and indefinite in that it is not known what is meant by the variables Y', Z', Q' and R_4' in formula IX which are not defined within the claim.

xx. Claim 17 is vague and indefinite in that it is not known what is meant by the variables R_1', R_2' and R_3' in formula X which are not defined within the claim.

yy. Claim 17 is vague and indefinite in that it is not known what is meant by the variables R_1', R_2', R_3', Y', Z', Q' and R_4' in formula XI which are not defined within the claim.

zz. Claim 17 is vague and indefinite in that it is not known what is meant by -D- in formula XI, indicating a divalent moiety, however, D is defined as a substituent which is monovalent.

aaa. Regarding claim 17, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

bbb. Claim 17 is vague and indefinite in that it is not known what is meant by the variables Y, Z, Q and R4 in formula XII which are not defined within the claim.

ccc. Claim 17 is vague and indefinite in that it is not known what is meant by the variables R1, R2 and R3 in formula X which are not defined within the claim.

ddd. Claim 17 is vague and indefinite in that it is not known what is meant by the two different formula X.

eee. Claim 17 is vague and indefinite in that it is not known what is meant by “nitrogen carrying optional substituents” in the definition of W.

fff. Claim 17 is vague and indefinite in that it is not known what is meant by “optional substituents” in the definition of W'.

ggg. Regarding claim 17, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

hhh. Claim 17 is vague and indefinite in that it is not known what is meant by the variables R2, R3, X, Y, Z, Q and R4 in formula XV which are not defined within the claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 12, 14 and 15 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brenda L. Coleman/
Primary Examiner, Art Unit 1624